
4-Vinylcyclohexene

CAS #100-40-3

Swiss CD-1 mice, at 0.0, 100, 250, 500 mg/kg, gavage in corn oil

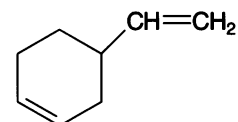
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Started 2/3/88; Completed 5/14/91

NTIS #PB91211250



4-Vinylcyclohexene (VCH) is used as the precursor of vinylcyclohexene dioxide, a reactive diluent in epoxy resins, and has few reproductive data available in the open literature. VCH was tested for its effects on reproduction and fertility in Swiss CD-1 mice using the RACB protocol (Grizzle et al., *Fundam Appl Toxicol* 22:122-129 [1994]). Data from a 2-week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 100, 250, 500 mg/kg by gavage in corn oil.

In the continuous cohabitation phase, four, one, one, and four mice died in the control through high dose groups, respectively. The causes of death were not considered by the veterinarian to be related to VCH exposure.

VCH did not reduce F_0 mouse body weights up through week 13 of the 18-week Task 2, and no fertility or reproductive measure was changed by VCH. Although pup weights were monotonically reduced (by $\leq 5\%$), the reduction was not significant.

Since no reproductive or developmental toxicity was found in Task 2, the last litter from all dose groups was reared to weaning, and pup weight and viability monitored. Exposure of the dams to VCH had no adverse effect on pup number or growth to weaning. Only the control and high dose mice were kept and dosed until the second generation mating trial at approximately postnatal day 74.

Gavage with the high dose of VCH had no effect on the fertility of the mice; numbers of pups per litter were not changed, but adjusted live F_2 pup weight was significantly reduced by approximately 5%. Postpartum dam weight was also reduced by approximately 8%, compared to controls.

After the F_2 pups were delivered and evaluated, the F_1 adults were killed and necropsied. The high dose males weighed approximately 7% less than their respective controls, while adjusted liver weight was increased by approximately 9%. The number of spermatids per milligram of testis was approximately 17% lower in the treated

mice. Sperm motility in the controls was aberrantly low (69% motile), while the VCH-exposed males had motility of approximately 85%, which is well within the historic control range for this laboratory. High dose female body weight was reduced by approximately 8% compared to controls, while relative liver weight was increased by the same amount. While estrous cycle length was not changed in the VCH-exposed mice, VCH was found to have induced significant oocyte death. The number of primary, growing, and antral follicles in step-sectioned ovaries from these high dose mice were reduced by approximately 34, 55, and 35%, respectively. In this light, the similarity of litter size in treated and control F_1 mice is notable. There were no treatment-related microscopic lesions.

Thus, this study showed that 4-vinylcyclohexene caused some gonadal toxicity in the second generation (fewer spermatids and fewer oocytes) and reduced F_2 pup weights, concomitant with small increases in adjusted liver weight.

4-VINYLCYCLOHEXENE

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB91211250

Chemical: 4-Vinylcyclohexene

CAS#: 100-40-3

Mode of exposure: Gavage

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	100 mg/kg	250 mg/kg	500 mg/kg
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	—, ↓
Kidney weight ^a		•	•	•
Liver weight ^a		•	•	•
Mortality		—, —	—, —	—, —
Feed consumption		—, —	—, —	—, —
Water consumption		—, —	—, —	—, —
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight ^a	•	•	•
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F ₁ generation	Dose concentration →	100 mg/kg	250 mg/kg	500 mg/kg
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		—, —	—, —	—, —
Mortality		—, —	—, —	—, —
Adult body weight		•	•	↓, ↓
Kidney weight ^a		•	•	—, —
Liver weight ^a		•	•	↑, ↑
Feed consumption		•	•	↑, ↑
Water consumption		•	•	—, —
Clinical signs		•	•	—

Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•	•	—, ↓
Absolute testis, epididymis weight ^a	•	•	—, —
Sex accessory gland weight ^a (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	250 mg/kg
NOAEL general toxicity:	250 mg/kg
F ₁ more sensitive than F ₀ ?	Yes
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.